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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,969	09/25/2000	Johannes M. Van Noort	101137-4	3142

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EXAMINER
SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/14/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/668,969	VAN NOORT ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 5 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 5 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08975696 .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Claim 5 is under consideration. Claims 1-4 have been cancelled.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. The specification fails to provide guidance as to how to use the claimed method for the treatment of disease in vivo in humans. The only disclosed use for the claimed method is the treatment of disease in vivo in humans. The only apparent substantive use for the claimed method is the treatment of disease in vivo in humans.

Although the amino acid sequence of alpha B crystallin is disclosed in the specification (see Figure 3, of the specification, in particular), there is no evidence of record would indicate that the claimed invention can be used to treat disease in vivo in humans. Applicant has provided no examples using alpha B crystallin to treat disease in humans or any animal model. While alpha B crystallin was administered to mice in the specification, section 2.3 (pages 37-39), no disease was actually treated in said mice. Besides the identification of alpha B crystallin in myelin from patients with multiple sclerosis, which was previously taught by Iwaki, et al., ((W) see page 346, Table 1, in particular), and Murayama, et al. ((X) see page 32, col. 2, paragraph 2, in particular), the specification fails to provide guidance as to how to use the claimed alpha B crystallin for therapy of autoimmune disorders or for patients with multiple sclerosis. Typically, an autoimmune disease is diagnosed at the time of onset when significant tissue damage has already occurred. Furthermore, Tisch et al., teach that treating an ongoing T-cell-mediated autoimmunity by administering an antigen peptide may have an immunizing effect and exacerbate the disease condition (page 437, column 3, in particular). How the antigen is administered is also a key factor in determining whether

an immunogenic or toleragenic response is induced. The duration of the toleragenic effect is an additional factor. Additionally, the high degree of specificity required for the process of clonal deletion/anergy may be limiting when dealing with diseases such as MS, in which there are responses to several antigens (see page 437, col. 2 ¶ 3 and bridging over to col. 3, ¶ 4). Wraith et al. teach the "Inhibition of the response restricted by one class II molecule may lead only to the escape to an autoimmune response to a separate epitope restricted by a different class II molecule." (see page 253 column 1, in particular). Therefore, since the applicant has given no guidance as to how their peptide specific therapy would overcome autoreactive T cell escape mechanisms in humans or whether the peptide would induce autoimmunity or tolerance, and because there is no evidence of record to show that one skilled in the art would associate the said detection of alpha B crystallin in myelin from patients with multiple sclerosis with the successful therapeutic treatment claimed herein, it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention and this is not sanctioned by the statute. In addition, Spack teaches that attempts to treat MS via inducing oral tolerance to myelin protein have been unsuccessful (see abstract). Thus, it is recognized in the art that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute. Undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification. See In re Wands 8 USPQ2d 1400(CAFC 1988).

Regarding applicants comments, the use for the claimed invention disclosed in the specification is treatment of MS. The specification provides no evidence that the claimed method can be used to treat a disease in vivo in humans or any animal model. While alpha B crystallin was administered to mice in the specification, section 2.3 (pages 37-39), no disease was actually treated in said mice. The various references cited in the instant rejection explain why it would be unpredictable in the absence of appropriate evidence as to whether the instant invention could be used to treat disease in vivo in humans. In addition, Spack teaches that attempts to treat MS via inducing oral tolerance to myelin protein have been unsuccessful (see abstract). Regarding applicants comments about antigenic peptides, the comments in the instant rejection

apply to administered peptides or proteins. The art recognizes that all antigens derived from proteins which are recognized by T cells are subjected to antigen processing wherein the T cells recognize small peptides presented by the appropriate MHC allele.

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1900~~ 1644

Ron Schwadron, Ph.D.
Primary Examiner
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